

## REMARKS

### In the Claims:

Claims 3, 5-7, and 23-25 are pending. Claims 3 and 24 are amended herein for purposes of increasing the clarity of the claims. Specifically, Claims 3 and 24 are amended herein to clarify that the claimed method involves selecting a maturation stage of an *Echinacea* plant that has a standardized concentration of marker compound. No new matter is added by this amendment and support for the amendment may be found throughout the specification including at paragraphs 0002, 0005, 0017, 0024, 0025, 0032, 0033, Table 1 on page 6 and original claims 10, 12, 15, and 18.

### Claim Objections:

Claim 3 is objected to because allegedly a period is omitted at the end of the claim. Applicants respectfully submit that the end of the claim does have the proper period punctuation but have added a semi-colon to Claims 3 and 24 in order to further clarify the punctuation and form of the claims.

### Claim Rejections:

#### 35 U.S.C. § 112, ¶ 1:

Claims 3, 5-7, and 23-25 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. Specifically, the Office action alleges that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors were in possession of the claimed invention because the phrase "greater than zero" as present in Claims 3 and 24 is alleged to be new matter. While Applicants respectfully disagree with this ground of rejection, to expedite prosecution, Applicants have herein amended Claims 3 and 24 to delete the phrase "greater than zero" as it relates to the concentration of marker compound. Applicants have therefore overcome this ground of rejection and respectfully request that it be withdrawn.

**35 U.S.C. § 112, ¶ 2:**

Claims 3, 5-7, and 23-25 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Office action alleges that the claims are indefinite because they do not recite a level of marker compound.

Applicants respectfully disagree with this ground of rejection. To expedite prosecution, Applicants have herein further clarified that the claimed methods are directed to a standardized concentration of a marker compound. One of ordinary skill in the art would know the metes and bounds of a standardized concentration of marker compound. According to Section 2173.05(b) of the MPEP that is sufficient: the "[a]cceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification."

More specifically, standardization of extracts has a well-understood meaning. A standardized concentration of a marker compound merely means that each extract having a standardized concentration of a marker compound has the same concentration of that marker compound. Thus, for standardization, the important aspect is that the level of marker compound remains consistent from extract to extract. For example, chicoric acid is a marker compound commonly used to standardize *Echinacea* extracts. Standardization of an *Echinacea* extract to a concentration of chicoric acid ensures that each preparation of *Echinacea* contains the same amount of chicoric acid.

Plant extracts for pharmaceutical and medicinal purposes are commonly standardized as a means of ensuring uniformity. Furthermore, as paragraph 0025 of the specification explains, "standardization to a marker such as chicoric acid is important to meet regulatory expectations." Standardization ensures that each herbal extract contains equal amounts of the marker compound. Indeed, standardization provides for uniformity in extracts from a single provider, such as the present Assignee, Access

Business Group International. As stated in the response to Office action dated September 17, 2007, "for standardization, the most important attribute is that all extracts from a single source (e.g. a single provider) have the **same** concentration..." within a statistically acceptable margin of error.

The present application provides an example that describes using chicoric acid as a marker compound for an *Echinacea* extract and thereby illustrates the principle that each preparation of *Echinacea* extract must have the same concentration of marker compound. Specifically, Table 1 and paragraphs 22 and 24 of the present application report that the levels of chicoric acid do not vary greatly in *Echinacea* from plant to plant or maturation stage to maturation stage. Indeed, the values reported at Table 1 range from  $3.49 \pm 0.09$  % to  $3.54 \pm 0.14$  %. As stated in paragraph 24, the variations are within levels generally accepted by those skilled in the art to be variations between individual plants. Thus, one of ordinary skill in the art, in view of the specification, will understand what is claimed by "standardized concentration of a marker compound." No more is required. This ground of rejection is overcome and Applicants respectfully request that it be withdrawn.

Claim 3 is also rejected under 35 U.S.C. § 112, second paragraph because the recitation of the phrase "the medicinal plant" lacks an antecedent basis. Claim 3 is amended herein replace "the medicinal plant" with "the *Echinacea*" and Claim 24 is amended to replace "the plant" with "the *Echinacea* plant" to clarify that the claimed method is directed to preparing a standardized extract of the *Echinacea* plant. Applicants have overcome this ground of rejection and respectfully request that it be withdrawn.

### 35 U.S.C. § 103

Finally, Claims 3, 5-7, and 23-25 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of A in view of C or B in view of C, wherein A =

Seidler-Lozykowska et al. (2003), B = Dou et al. (2001 – Abstract) and C = Rininger et al. (2000).

Applicants respectfully disagree with this ground of rejection. According to Section 2141 of the MPEP, which is consistent with the Supreme Court's recent decision in *KSR Internat'l Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007), when determining whether a claimed invention is obvious under 35 U.S.C. § 103, the following tenets of patent law must be adhered to:

- (A) The claimed invention must be considered as a whole;
- (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;
- (C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and
- (D) Reasonable expectation of success is the standard with which obviousness is determined.

*Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986).

When these tenets of patent law are properly applied, it is clear that the claimed invention is not obvious in view of the cited references.

First, the claimed invention as a whole is a method for determining optimal harvest window of *Echinacea* based on selecting a plant maturation stage that has both a standardized concentration of a marker compound and immunostimulatory activity. The claimed method also includes a step of preparing a standardized extract at that selected maturation stage.

The cited references as a whole do not teach this method. Specifically, two of the cited references, Seidler-Lozykowska and Dou, examine when the greatest levels of typical marker compounds (i.e. polyphenolics, phenolic acids such as chicoric acid, caffeic

acid, etc.) used to standardize extracts may be obtained and from which specific parts of the plant they may be obtained. Neither Seidler-Lozykowska nor Dou discuss any immunopotentiating activity of *Echinacea*. The third cited reference, Rininger, teaches that standardized *Echinacea* extracts do not exhibit immunostimulatory activity.

According to the Office action, Applicants have over-generalized the Rininger reference. Applicants respectfully disagree. Rininger analyzed whether extracts standardized to a 4% concentration of phenolic marker compound exhibited immunopotentiating activity. Rininger clearly teaches that the analyzed standardized extracts were "inactive" for immunostimulatory activity. See Rininger at page 8,10. In addition, Rininger analyzed compounds, including chologenic acid and chicoric acid, which are commonly used as standardized marker compounds for *Echinacea* extracts. Rininger clearly teaches that those compounds commonly used as standardized marker compounds for *Echinacea* extracts were not found to possess any immunostimulatory activity. *Id.* Indeed, Rininger explicitly teaches, "standardized *Echinacea* extracts as well as purified chemical standards for the production of *Echinacea* extracts were found to be inactive for these immunomodulatory functions." *Id.* at page 10. This teaching is consistent with Rininger's analysis of non-standardized extracts. Specifically, Rininger analyzed non-standardized *Echinacea* extracts, specifically *Echinacea* herb and root powders, and found the non-standardized extracts possessed immunostimulatory activity. *Id.* at page 7-8. Thus, at a minimum, one of ordinary skill in the art may fairly conclude from these teachings of Rininger — that *Echinacea* extracts standardized to 4% phenolic acids are not immunostimulatory, that marker compounds commonly used to standardize *Echinacea* extracts do not provide any immunostimulatory activity to an *Echinacea* extract, and that non-standardized *Echinacea* extracts do exhibit immunostimulatory activity — that standardized *Echinacea* extracts do not necessarily or always exhibit immunopotentiating activity and may not exhibit any such activity.

The Office action mischaracterizes the teaching of Rininger regarding the immunopotentiating activity of polysaccharides from *Echinacea*. The portion of Rininger relied on by the Office action simply references journal articles and studies by other

groups. Indeed, although Rininger references these other studies, stating that "[l]aboratory studies have shown that *Echinacea purpurea* herb and purified polysaccharides from *Echinacea purpurea* cell cultures possess immunostimulatory activity....," Rininger in fact calls into question these results. *Id.* at 2. Specifically, Rininger states that "[h]owever, the polysaccharides purified from *Echinacea* cell cultures may be different than ones endogenously found in the plant." *Id.* Rininger therefore teaches the importance of analyzing the entire preparation of *Echinacea* to determine immunostimulatory activity, and in fact, presents results from its analysis of preparations of *Echinacea* plant herb and root powders as well as the standardized *Echinacea* extract. Furthermore, Rininger did test chlorogenic acid as an individual compound and found that it was negative for macrophage activation. See *Id.* p. 8. Rininger additionally tested full spectrum extracts containing polysaccharides and phenolic compounds which were also found to be inactive in the macrophage activation assay. *Id.* Thus, taken as a whole, Rininger teaches away from a conclusion that standardized *Echinacea* extracts and the common marker compounds used for standardization of *Echinacea* extracts exhibit immunostimulatory activity.

Seidler-Lozykowska and Dou both teach one of ordinary skill in the art to produce *Echinacea* extracts with the highest concentration of polyphenolic acids and chicoric acid, respectively, which are compounds commonly used to standardize *Echinacea* extracts. Rininger teaches that neither standardized *Echinacea* extracts nor marker compounds commonly use to standardize *Echinacea* extracts, *i.e.* chlorogenic acid and/or chicoric acid, exhibit immunostimulatory activity. These references cannot be combined to render the claimed invention obvious because the combined teaching is that standardized *Echinacea* extracts and/or the marker compounds used to standardize the extracts do not exhibit immunostimulatory activity.

Indeed, there is no consensus on which phytochemical constituents of *Echinacea* are active. Barrett, B., *Medicinal properties of Echinacea: A critical review*, *Phytomedicine* 10: 66, 69 (2003). The specification at paragraph 0017 states that no definitive connection exists between any specific marker compound alone having an observed

immunomodulating activity. The greatest concentration of a marker compound does not necessarily correspond to the highest level of immune-stimulatory product. Claims 3 and 24, which provide a method for determining the optimal harvest window of *Echinacea* plants, requires a concentration of marker compound for preparing a standardized extract of the *Echinacea* plant having a highest level of immune-stimulatory product. Therefore, the claims are nonobvious in view of Rininger, alone or in combination with Dou and/or Seidler-Lozykowska.

Applicants respectfully submit that when the claims are considered in their entirety and when the references also are considered as a whole, without relying on impermissible hindsight, it is clear that the cited references do not provide any reasonable expectation of success in formulating a method for determining optimal harvest window of *Echinacea*, based on selecting a plant maturation stage that has both a standardized concentration of a marker compound that is obtained from the preparation of *Echinacea* plant for preparing a standardized extract and immunostimulatory activity. Specifically, Seidler-Lozykowska and Dou both teach means for producing *Echinacea* extracts with the highest concentration of compounds used to standardize *Echinacea* extracts. Rininger teaches that neither standardized *Echinacea* extracts nor the common marker compounds used for standardization of *Echinacea* extracts exhibit immunostimulatory activity. Thus, one of ordinary skill in the art would not, based on the teachings of the cited references, expect the claimed method of optimizing harvest window of a plant, e.g. *Echinacea*, by selecting a plant maturation stage that has a standardized concentration of a marker compound, yet also maintains immunostimulatory activity, to be successful.

Claims 3, 5-7, and 23-25 are not obviousness in view of the cited references. Applicants have overcome this ground of rejection and respectfully request that it be withdrawn.

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**SUMMARY**

Applicants believe that currently pending claims 3, 5-7, and 23-25 are patentable. The Examiner is invited to contact the undersigned attorney for Applicants via telephone if such communication would expedite allowance of this application.

Respectfully submitted,



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